REVIEW PAPER

Age and Anti-Müllerian Hormone as Predictors of Oocyte Outcomes: Bridging the Gap Between Pre-Retrieval Expectations and Post-Retrieval Reality — A Comprehensive Review

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ABSTRACT
Accurate prediction of oocyte quantity and quality remains a complex challenge due to inherent biological variability and limitations of predictive indicators. Among available predictors, age and Anti-Müllerian Hormone (AMH) are widely used indicators for estimating ovarian response. While these markers provide valuable insights, discrepancies between pre-retrieval expectations and post-retrieval outcomes remain a persistent challenge. Evidence suggests that although these indicators demonstrate moderate predictive value at a population level, their precision at the individual level is limited due to significant biological variability. [1,2] This review critically examines the role of age and AMH in predicting oocyte outcomes, highlighting the gap between expected and observed results and discussing future directions for improved predictive modelling.

Keywords: Age, Anti-Müllerian Hormone, Oocyte Quality, Predictive Models, Variability

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INTRODUCTION

Accurate prediction of oocyte quantity and quality prior to retrieval represents a fundamental aspect of reproductive biology and outcome optimization. The ability to anticipate ovarian response not only facilitates better planning and expectation setting but also provides critical insights into the underlying biological processes governing follicular development and oocyte competence. Despite significant advancements in predictive methodologies, achieving consistent and reliable prediction remains a considerable challenge. Among the various predictors proposed, age and Anti-Müllerian Hormone (AMH) have emerged as the most widely utilized indicators of ovarian reserve and response. Age is universally recognized as a primary determinant of reproductive potential, reflecting both the progressive depletion of the ovarian follicular pool and the decline in oocyte quality over time.[7] This age-related decline is characterized by a reduction in oocyte number as well as an increase in chromosomal abnormalities and compromised cellular function, ultimately affecting developmental competence.[8,10] AMH, produced by granulosa cells of pre-antral and small antral follicles, serves as a quantitative biomarker of ovarian reserve and has gained widespread acceptance due to its relative stability across the menstrual cycle and its strong association with follicular pool size.[11,12] Numerous studies have demonstrated a positive correlation between AMH levels and oocyte yield, making it a valuable tool for predicting ovarian response.[3,4] However, while AMH effectively reflects the quantity of oocytes, its ability to predict oocyte quality remains limited, thereby restricting its utility as a comprehensive predictive marker.

Despite the established roles of age and AMH, a persistent challenge in reproductive prediction lies in the discrepancy between pre-retrieval expectations and post-retrieval outcomes. Predictive models based on these indicators often demonstrate moderate correlation with observed outcomes at a population level; however, their predictive precision at an individual level is frequently inadequate.[1,5] This discrepancy highlights an important limitation of current predictive approaches; wherein statistical associations do not necessarily translate into accurate outcome prediction. A critical distinction in this context is between correlation and accuracy. While correlation measures the strength of association between variables, accuracy reflects the ability to predict exact outcomes. Moderate correlations, as reported in several studies, indicate that predictive indicators can identify general trends but are insufficient for precise individual-level prediction. Consequently, a significant proportion of cases exhibit either overestimation or underestimation of oocyte outcomes, reflecting substantial biological variability.[5] The variability observed in oocyte outcomes can be attributed to multiple factors, including intrinsic ovarian heterogeneity, differences in follicular dynamics, genetic influences, and environmental factors. Furthermore, current predictive models are limited by their reliance on a narrow set of measurable parameters, which fail to capture the complex and dynamic nature of folliculogenesis and oocyte maturation.

In recent years, there has been growing recognition of the need to move beyond single-parameter prediction models toward more integrative approaches that consider multiple biological variables simultaneously. While combining age and AMH improves predictive performance, significant variability persists, suggesting that additional factors must be incorporated to achieve meaningful improvements in prediction accuracy.[2] In this context, the present review aims to critically examine the roles of age and AMH as predictors of oocyte quantity and quality, with a particular focus on the gap between pre-retrieval expectations and post-retrieval reality. By synthesizing existing evidence and analyzing the limitations of current predictive models, this review seeks to highlight the challenges associated with prediction variability and to explore potential directions for developing more accurate and individualized predictive frameworks.

OOCYTE BIOLOGY AND FOLLICULOGENESIS

Oocyte development is a highly coordinated and complex biological process governed by the dynamics of folliculogenesis. The ovarian reserve is established during fetal life, with a finite number of primordial follicles that progressively decline throughout the reproductive lifespan. This irreversible depletion forms the biological basis of reproductive ageing and significantly influences both oocyte quantity and quality.[7] Folliculogenesis involves the transition of primordial follicles into primary, secondary, and subsequently antral follicles under tightly regulated endocrine and paracrine signaling mechanisms. The initial recruitment of primordial follicles is largely gonadotropin-independent and occurs continuously, while the later stages of follicular growth are dependent on follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The number of follicles that successfully progress to the antral stage determines the pool of recruitable follicles and ultimately influences oocyte yield.[11,13]

A critical aspect of folliculogenesis is the selection of a dominant follicle from a cohort of developing follicles. This selection is influenced by hormonal gradients, intra-ovarian signaling pathways, and follicular sensitivity to gonadotropins. However, this process is inherently variable, contributing to differences in ovarian response among individuals with similar baseline characteristics.[5]

Oocyte quality is determined by both nuclear and cytoplasmic maturation. Nuclear maturation involves the completion of meiosis, ensuring chromosomal integrity, while cytoplasmic maturation encompasses mitochondrial function, organelle distribution, and accumulation of essential molecular factors required for early embryonic development. Disruptions in these processes can result in reduced developmental competence, even in the presence of adequate oocyte numbers.[9,10] Mitochondrial function plays a particularly important role in oocyte quality, as mitochondria provide the energy required for meiotic progression and early embryogenesis. Age-related mitochondrial dysfunction has been identified as a key factor contributing to declining oocyte quality. Similarly, increased oxidative stress and accumulation of reactive oxygen species can impair cellular integrity and compromise oocyte viability.[10] The microenvironment within the ovarian follicle also plays a significant role in determining oocyte competence. Granulosa cells, through bidirectional communication with the oocyte, regulate nutrient exchange, hormonal signaling, and local growth factor activity. Anti-Müllerian Hormone (AMH), secreted by granulosa cells of pre-antral and small antral follicles, acts as a regulator of follicular recruitment and reflects the size of the growing follicular pool.[11,12]

Despite the structured progression of folliculogenesis, considerable inter-individual variability exists in follicular recruitment, growth rate, and oocyte maturation. This variability is influenced by genetic factors, endocrine environment, and intrinsic ovarian biology. As a result, individuals with similar age and AMH levels may exhibit markedly different oocyte outcomes.[5,15] The complexity of folliculogenesis underscores the limitations of predictive models based solely on a few measurable indicators. While markers such as age and AMH provide useful approximations of ovarian reserve, they do not fully capture the dynamic and multifactorial nature of oocyte development. Consequently, variability in oocyte quantity and quality remains an inherent feature of biological systems, contributing to the gap between predicted and observed outcomes.

IMPACT OF AGE ON OOCYTE QUANTITY AND QUALITY

Age is one of the most critical determinants of ovarian function and reproductive potential, exerting a profound influence on both the quantity and quality of oocytes. The effects of ageing on the ovary are multifactorial, involving progressive depletion of the follicular pool, alterations in hormonal regulation, and deterioration in cellular and molecular integrity of oocytes.[7]

Decline in Ovarian Reserve

The most prominent effect of advancing age is the gradual depletion of the ovarian reserve. Females are born with a finite number of primordial follicles, which decline continuously due to atresia throughout life. This depletion accelerates with increasing age, particularly after the mid-30s, resulting in a marked reduction in the number of recruitable follicles.[7]

Studies have demonstrated that the decline in follicle number is not linear but exponential, leading to significant inter-individual variability in ovarian ageing. Consequently, individuals of similar chronological age may exhibit markedly different ovarian reserves, highlighting the limitations of age as a sole predictor of oocyte quantity.[1]

Decline in Oocyte Quality

In addition to quantitative decline, ageing is associated with a significant deterioration in oocyte quality. This decline is primarily attributed to increased rates of chromosomal abnormalities, impaired meiotic spindle formation, and mitochondrial dysfunction.[8,10]

Age-related aneuploidy is a well-documented phenomenon, resulting from errors in chromosomal segregation during meiosis. Franasiak et al. demonstrated a progressive increase in aneuploidy rates with advancing maternal age, which directly impacts oocyte competence and developmental potential.[8]

Mitochondrial dysfunction further contributes to reduced oocyte quality. As mitochondria are essential for ATP production, their decline leads to impaired energy metabolism, affecting meiotic progression and early embryonic development. Increased oxidative stress and accumulation of reactive oxygen species exacerbate cellular damage, further compromising oocyte viability.[10]

Hormonal and Endocrine Changes

Ageing is also associated with alterations in the endocrine environment of the ovary. Changes in gonadotropin dynamics, including increased basal follicle-stimulating hormone (FSH) levels and altered feedback mechanisms, reflect declining ovarian function.

These hormonal changes influence follicular recruitment and maturation, contributing to variability in ovarian response. However, hormonal markers alone are insufficient to fully capture the complexity of age-related changes in oocyte development.[2]

Variability in Age-Related Decline

Although age is a strong determinant of reproductive potential, significant variability exists in the rate and pattern of ovarian ageing. Factors such as genetic predisposition, environmental influences, lifestyle factors, and underlying physiological differences contribute to this variability.[7] This heterogeneity explains why individuals of similar age may exhibit divergent oocyte outcomes. Some individuals maintain relatively preserved ovarian function despite advancing age, while others experience early decline. This variability limits the predictive accuracy of age-based models and contributes to discrepancies between expected and observed outcomes.

Implications for Predictive Modelling

The influence of age on oocyte outcomes underscores its importance as a predictive parameter; however, its limitations must be recognized. While age provides a general estimate of ovarian reserve and oocyte quality, it lacks precision at the individual level due to inherent biological variability.

Consequently, predictive models relying solely on age are insufficient for accurate outcome prediction. Integrating age with other biomarkers, such as AMH, improves predictive performance but does not eliminate variability. This highlights the need for multi-factorial approaches in predictive modeling.[2,5]

ANTI-MÜLLERIAN HORMONE AS A BIOMARKER

Anti-Müllerian Hormone (AMH) has emerged as one of the most reliable and widely utilized biomarkers for assessing ovarian reserve. Secreted by granulosa cells of pre-antral and small antral follicles, AMH reflects the size of the growing follicular pool and provides an indirect measure of the remaining ovarian reserve.[11,12]

Physiological Role of AMH

AMH plays a crucial role in regulating folliculogenesis by inhibiting the initial recruitment of primordial follicles and modulating follicular sensitivity to follicle-stimulating hormone (FSH). This regulatory function helps maintain the longevity of the ovarian reserve and prevents premature depletion of the follicular pool.[12] Unlike other hormonal markers, AMH levels remain relatively stable throughout the menstrual cycle, making it a convenient and reliable biomarker for clinical and research purposes.[11]

AMH and Oocyte Quantity

A strong positive correlation has been consistently demonstrated between AMH levels and oocyte yield. Higher AMH levels are generally associated with a greater number of recruitable follicles and increased oocyte retrieval.[3,4] Several studies have validated AMH as a superior predictor of ovarian response compared to traditional markers such as basal FSH or estradiol levels.[13] This makes AMH a cornerstone parameter in predictive models aimed at estimating oocyte quantity.

AMH and Oocyte Quality

Despite its strong association with oocyte quantity, the role of AMH in predicting oocyte quality remains controversial. While some studies suggest a potential association, the majority of evidence indicates that AMH is primarily a quantitative marker and does not reliably predict oocyte competence or developmental potential.[4] This limitation arises because oocyte quality is influenced by multiple factors, including chromosomal integrity, mitochondrial function, and intracellular processes, which are not directly reflected by AMH levels.

Limitations of AMH as a Predictive Marker

Although AMH is widely used, several limitations must be considered:

(i) Inter-individual variability in AMH levels
(ii) Differences in assay methodologies
(iii) Lack of direct correlation with oocyte quality
(iv) Influence of external and physiological factors

These limitations highlight that while AMH is a valuable predictor, it should not be used in isolation for outcome prediction.

Implications for Predictive Modelling

AMH serves as a robust indicator of ovarian reserve and oocyte quantity; however, its predictive utility is enhanced when combined with other parameters such as age. Even then, variability persists, indicating that AMH-based models cannot fully account for the complexity of ovarian response.[2,5]

PRE-RETRIEVAL EXPECTATIONS

The formulation of pre-retrieval expectations is primarily grounded in established associations between baseline predictors and ovarian response. Age reflects the biological status of the ovarian reserve and is inversely associated with both oocyte quantity and quality.[7] In contrast, AMH serves as a quantitative marker of the growing follicular pool and demonstrates a strong positive correlation with oocyte yield.[3,4] Based on these relationships, predictive assumptions are typically structured as follows:

(i) Younger age is associated with higher oocyte quantity and better quality

(ii) Higher AMH levels indicate increased ovarian reserve and expected oocyte yield

(iii) Advanced age is associated with diminished ovarian response and reduced oocyte competence

These assumptions are supported by multiple studies demonstrating moderate correlations between these indicators and ovarian outcomes at a population level.[1,2]

Predictive Models and Statistical Frameworks

Pre-retrieval expectations are often derived from statistical models incorporating age, AMH, and, in some cases, additional parameters such as baseline hormonal profiles. These models aim to estimate expected oocyte yield and provide a probabilistic assessment of ovarian response.

Most predictive models rely on regression-based approaches, wherein age and AMH are treated as independent variables influencing oocyte outcomes. While such models demonstrate reasonable predictive performance at a population level, they inherently assume homogeneity in biological response, which does not hold true in real-world settings.[2]

Furthermore, these models are largely based on population averages, and their applicability to individual cases is limited. As a result, while predictions may align with overall trends, significant deviations are often observed at the individual level.

Standardization of Expectations

In practice, pre-retrieval expectations are often standardized into categorical interpretations based on AMH levels and age groups. For instance:

(i) Low AMH levels are associated with expected poor response

(ii) Moderate AMH levels indicate average response

(iii) High AMH levels suggest increased oocyte yield

Similarly, age stratification is used to estimate expected decline in ovarian reserve and quality. While such standardization simplifies interpretation, it may oversimplify complex biological processes and fail to account for inter-individual variability.[11,12]

Limitations of Pre-Retrieval Expectations: Despite their widespread use, pre-retrieval expectations are subject to several inherent limitations:

Over-Reliance on Limited Parameters: Most predictive models rely heavily on age and AMH, which, although informative, do not fully capture the multifactorial nature of folliculogenesis and oocyte maturation.

Inability to Capture Biological Variability: Intrinsic differences in ovarian physiology, follicular dynamics, and cellular processes result in variability that cannot be explained by baseline indicators alone.[5]

Assumption of Linear Relationships: Predictive models often assume linear relationships between variables and outcomes, whereas biological processes are inherently nonlinear and dynamic.

Variability in Measurement and Interpretation: Differences in assay techniques, laboratory standards, and interpretation thresholds for AMH may further contribute to inconsistencies in prediction.[12]

Implications for Predictive Accuracy: The limitations outlined above contribute to a key challenge in predictive modelling: the distinction between statistical association and actual predictive accuracy. While age and AMH demonstrate statistically significant correlations with oocyte outcomes, their ability to accurately predict individual outcomes remains limited.

This discrepancy results in frequent mismatches between expected and observed outcomes, manifesting as overestimation or underestimation of oocyte yield. Such variability highlights the probabilistic nature of predictive models and underscores the need for cautious interpretation of pre-retrieval expectations.

Role in the Expectation–Reality Framework

Pre-retrieval expectations form the reference point against which post-retrieval outcomes are evaluated. The gap between these expectations and actual observations represents a critical area of analysis in understanding predictive limitations. Evidence suggests that while predictive indicators provide useful approximations, their reliability is constrained by underlying biological variability and incomplete modelling of complex processes.[4,5] This forms the basis for examining the divergence between expected and observed outcomes in subsequent sections.

POST-RETRIEVAL REALITY

Post-retrieval outcomes represent the actual biological response and serve as the basis for evaluating the accuracy of pre-retrieval predictions. Despite the widespread use of age and Anti-Müllerian Hormone (AMH) as predictive indicators, considerable variability is observed between expected and actual oocyte outcomes. Several studies have demonstrated that while age and AMH show moderate correlation with oocyte yield, their predictive accuracy at the individual level remains limited.[4,5] Individuals with similar baseline characteristics often exhibit markedly different oocyte responses, highlighting the inherent variability of ovarian function. In practical settings, post-retrieval outcomes frequently demonstrate distinct patterns of deviation from expected estimates. These include unexpectedly high or low oocyte yield, inconsistent oocyte quality despite similar predictive parameters, and variable response across individuals with comparable age and AMH levels. Such observations emphasize that predictive indicators are unable to fully account for the complexity of ovarian response.

A key feature of post-retrieval reality is the frequent mismatch between predicted and observed outcomes, which may manifest as either overestimation or underestimation of oocyte yield. This reflects the probabilistic rather than deterministic nature of current predictive models.[5] Consequently, predicted values should be interpreted as approximate estimates rather than exact outcomes.

The discrepancy between expected and actual outcomes can be attributed to the multifactorial nature of ovarian response. While age and AMH provide an estimate of ovarian reserve, they do not fully capture dynamic biological processes such as follicular recruitment, intra-ovarian signalling, and cellular competence. As a result, a substantial proportion of variability in oocyte outcomes remains unexplained by these markers alone.[2,15] Taken together, these findings indicate that post-retrieval outcomes must be interpreted within the context of inherent biological variability. Age and AMH should therefore be regarded as probabilistic indicators that define a range of expected responses, rather than precise predictors of individual outcomes. This reinforces the need for cautious interpretation of pre-retrieval expectations and highlights the limitations of current predictive frameworks.

GAP BETWEEN EXPECTATION AND REALITY

A central theme emerging from the analysis of predictive indicators is the consistent gap between pre-retrieval expectations and post-retrieval outcomes. While age and Anti-Müllerian Hormone (AMH) are widely accepted as key predictors of ovarian response, their ability to accurately forecast individual outcomes remains limited. This discrepancy highlights a fundamental limitation of current predictive frameworks. At a population level, both age and AMH demonstrate statistically significant correlations with oocyte quantity, supporting their use as predictive markers.[1–3] However, these correlations do not translate into reliable individual-level predictions. In practice, a substantial proportion of cases exhibit divergence between expected and observed outcomes, manifesting as either overestimation or underestimation of oocyte yield.[4,5] This gap arises primarily from the distinction between statistical association and predictive accuracy. Correlation reflects the degree of relationship between variables, whereas predictive accuracy requires precise estimation of individual outcomes. Moderate correlations indicate that while general trends can be identified, individual variability remains largely unaccounted for.[5]

Key Issues Underlying the Expectation–Reality Gap

Several critical issues contribute to the persistent discrepancy between predicted and observed outcomes:

(i) Limited Predictive Scope of Age and AMH

Age and AMH, although essential, represent only partial indicators of ovarian biology. They primarily reflect ovarian reserve and expected quantity but do not fully capture oocyte competence or dynamic physiological processes.[2,15]

(ii) Over-Reliance on Simplified Models

Most predictive frameworks rely on linear, regression-based models that assume uniform biological response. Such simplifications fail to account for the nonlinear and adaptive nature of follicular development.

(iii) Inherent Biological Variability

Ovarian response is influenced by multiple interacting factors, including follicular dynamics, granulosa cell function, mitochondrial activity, and genetic variability. These factors introduce heterogeneity that cannot be explained by baseline indicators alone.[5]

(iv) Population-Based vs Individual Prediction

Predictive models are generally derived from population averages, which limits their applicability to individual cases. Individuals with similar age and AMH values may demonstrate markedly different outcomes, reflecting underlying biological diversity.

(v) Measurement and Interpretation Variability

Differences in assay techniques, laboratory standards, and threshold values for AMH interpretation may further contribute to inconsistencies in prediction.[12]

Implications of the Gap

The expectation–reality gap has important implications for predictive interpretation. Overestimation of oocyte yield may lead to unrealistic expectations, while underestimation may result in unnecessary pessimism. Recognizing the probabilistic nature of predictive indicators is therefore essential for appropriate interpretation.

Bridging the Gap

Addressing this discrepancy requires a shift toward more comprehensive predictive approaches. Incorporating additional biomarkers, genetic factors, and advanced analytical methods such as artificial intelligence may enhance predictive accuracy. Furthermore, moving toward personalized prediction models, rather than reliance on population averages, may help reduce variability and improve outcome prediction.

Summary

In summary, the gap between pre-retrieval expectations and post-retrieval outcomes reflects the inherent limitations of current predictive indicators. While age and AMH remain valuable tools, their predictive precision is constrained by biological complexity, variability, and incomplete modelling. Bridging this gap is essential for improving the reliability of predictive frameworks.

REASONS FOR PREDICTION VARIABILITY

The variability observed between pre-retrieval expectations and post-retrieval outcomes can be attributed to multiple interacting factors that are not fully captured by conventional predictive indicators such as age and Anti-Müllerian Hormone (AMH). These factors reflect the inherent complexity of ovarian biology and contribute significantly to the expectation–reality gap.

Biological Heterogeneity

One of the primary contributors to prediction variability is inter-individual biological heterogeneity. Even among individuals with similar age and AMH levels, differences in ovarian physiology, follicular dynamics, and cellular function can lead to markedly different oocyte outcomes.[5]

This variability limits the applicability of uniform predictive models.

Incomplete Representation of Ovarian Function

Age and AMH primarily reflect ovarian reserve and expected quantity but do not adequately capture other critical aspects of ovarian function, including oocyte competence, follicular microenvironment, and intracellular processes. As a result, predictive models based on these parameters remain inherently incomplete.[2,15]

Dynamic Nature of Folliculogenesis

Follicular recruitment and growth are dynamic processes influenced by endocrine and intra-ovarian signaling. These processes vary across individuals and cycles, leading to fluctuations in ovarian response that cannot be predicted using static baseline markers alone.[11]

Variability in Biomarker Measurement

Differences in assay techniques, laboratory standards, and interpretation thresholds for AMH can contribute to inconsistencies in prediction. Measurement variability may lead to discrepancies between estimated and actual ovarian reserve, thereby affecting predictive accuracy.[12]

Nonlinear and Multifactorial Relationships

Ovarian response is governed by nonlinear interactions among multiple biological variables. However, most predictive models assume linear relationships between predictors and outcomes, resulting in oversimplification and reduced accuracy.[2]

Influence of Unmeasured Factors

Several factors influencing oocyte outcomes remain unmeasured or inadequately quantified, including genetic predisposition, mitochondrial function, oxidative stress, and environmental influences. These factors contribute to unexplained variability in post-retrieval outcomes and limit the predictive power of current models.[10,15]

Implications for Predictive Reliability

The presence of these factors underscores the probabilistic nature of current predictive indicators. While age and AMH provide useful estimates at a population level, their ability to accurately predict individual outcomes is constrained by biological variability and incomplete modeling. Recognizing these limitations is essential for interpreting predictive estimates within an appropriate context.

COMBINED ROLE OF AGE AND AMH

The combined assessment of age and Anti-Müllerian Hormone (AMH) represents the most widely adopted approach for estimating ovarian response. Unlike individual predictors, their integration enables simultaneous evaluation of two distinct dimensions of ovarian function—biological ageing and follicular reserve—thereby offering a more contextualized understanding of expected outcomes. Rather than functioning as independent predictors, age and AMH interact to shape a response profile that cannot be adequately interpreted through either parameter alone. This interaction becomes particularly relevant in cases where the two indicators appear discordant. For instance, individuals with relatively preserved AMH levels despite advancing age may demonstrate adequate oocyte yield but variable quality, whereas younger individuals with diminished AMH may exhibit reduced quantity despite favorable age-related biological conditions. Such patterns highlight that predictive interpretation requires integration rather than isolated assessment.

The combined use of age and AMH improves the ability to stratify individuals into expected response categories and enhances predictive confidence at a broader level. However, this improvement primarily reflects better categorization rather than true precision. Even when both parameters are considered together, substantial variability persists in observed outcomes, indicating that their integration does not fully resolve the limitations of current predictive frameworks.[2,5] This residual variability underscores a critical insight: the combined model refines expectations but does not eliminate uncertainty. The persistence of mismatch between predicted and actual outcomes suggests that key determinants of ovarian response remain unaccounted for, including dynamic follicular behavior, cellular competence, and unmeasured biological influences.

Within the expectation–reality framework, the integration of age and AMH represents an advancement from simplistic prediction toward a more structured estimation approach. However, it still operates within the constraints of probabilistic modeling rather than deterministic prediction. As such, combined assessment should be interpreted as defining a likely range of outcomes rather than a precise forecast. In this context, the value of combining age and AMH lies not in achieving exact prediction, but in improving the contextual understanding of variability. Recognizing this limitation is essential for realistic interpretation and reinforces the central premise of this review—that even the most refined conventional predictors are inherently constrained by the complexity of ovarian biology.

FUTURE DIRECTIONS

The persistent gap between pre-retrieval expectations and post-retrieval outcomes highlights the need for a paradigm shift in predictive approaches. While conventional indicators such as age and Anti-Müllerian Hormone (AMH) provide valuable baseline information, future predictive frameworks must evolve to better capture the complexity and variability inherent in ovarian biology. A key direction lies in the development of multi-dimensional predictive models that integrate additional biological, biochemical, and functional parameters. Expanding beyond age and AMH to include factors such as follicular dynamics, cellular competence, and metabolic markers may improve the depth and reliability of prediction. Such integrative approaches are more likely to reflect the true biological processes governing oocyte outcomes.

Another important advancement is the application of data-driven and computational models, including machine learning techniques. These approaches can analyze complex, nonlinear relationships among multiple variables and identify patterns that are not apparent through traditional statistical methods. By incorporating large datasets and multidimensional inputs, such models hold promise for improving individualized prediction.

Future strategies should also emphasize a shift from point prediction to range-based estimation. Recognizing that biological outcomes inherently exhibit variability, predictive models should aim to define expected ranges rather than exact values. This approach aligns more closely with the probabilistic nature of ovarian response and allows for more realistic interpretation of outcomes.

Additionally, there is a need to move toward individualized prediction frameworks, wherein predictive estimates are tailored to the unique biological profile of each individual rather than derived solely from population averages. Personalized models that incorporate multiple layers of information may help reduce the mismatch between expected and observed outcomes.

Finally, future research should focus on standardization of predictive markers and methodologies, particularly with respect to AMH measurement and interpretation. Reducing variability in assessment techniques will improve consistency and enhance the comparability of predictive models across studies.

In summary, advancing predictive accuracy requires a transition from simplified, parameter-based models to integrative, dynamic, and individualized approaches. Bridging the gap between expectation and reality will depend on the ability of future models to capture the complexity of ovarian biology while acknowledging its inherent variability.

CONCLUSION

Age and Anti-Müllerian Hormone (AMH) remain the cornerstone predictors of oocyte quantity and ovarian response, providing a practical framework for estimating reproductive potential. However, as highlighted throughout this review, a consistent gap exists between pre-retrieval expectations and post-retrieval outcomes. While these indicators demonstrate meaningful associations at a population level, their predictive precision at the individual level is limited. This discrepancy reflects the inherent complexity and variability of ovarian biology, as well as the constraints of current predictive models that rely on a restricted set of parameters. The analysis of expectation–reality mismatch underscores a critical shift in perspective: predictive indicators should be interpreted as probabilistic tools that define a range of likely outcomes rather than precise determinants of response. Recognizing this limitation is essential for realistic interpretation and improved understanding of biological variability. The combined use of age and AMH enhances predictive context but does not eliminate uncertainty, reinforcing the need for more comprehensive and individualized predictive approaches. Future advancements must focus on integrating multiple biological dimensions and adopting models that better reflect the dynamic nature of ovarian response.

In conclusion, bridging the gap between expectation and reality requires not only improved predictive frameworks but also a conceptual shift in how prediction is understood—moving from certainty toward informed estimation within a variable biological system.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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